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# Lead Acetate Trihydrate

CAS #301-04-2

Swiss CD-1 mice, at 0.0, 0.125, 0.25, and 0.5% in water

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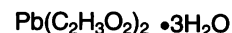
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NTIS #PB84208016

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Lead acetate trihydrate (PbA) was evaluated in this follow-up study as a possible reproductive toxicant using the RACB protocol (Morrissey et al., *Fundam Appl Toxicol* 13:747-777 [1989]). A previous study at the other RACB laboratory found significant toxicity at concentrations in the drinking water greater than or equal to 0.5%. Thus, levels for this study were set at 0.125, 0.25, and 0.5% weight per volume in drinking water. The highest level of PbA caused a slight (approximately 10%) reduction in water consumption, even though body weight was unaffected during Task 2. Based on measures of water consumption and body weights, these concentrations of PbA produced consumption estimates of approximately 200, 375, and 700 mg PbA/kg/day.

In the first generation (Task 2), one control female, one low dose female, four middle dose females, and seven females and one male at the high dose died during Task 2. These deaths were considered treatment related, but the cause of death

was not determined.  $F_0$  body weights were not affected by PbA consumption. There was a 7% decrease in adjusted live pup weight at the high dose, though PbA did not alter the number of litters per pair or the number of pups per litter.

Task 3 (the crossover study) was not conducted since there were no changes in pup number and only small changes in pup weight that were expected to be difficult to replicate in the single-mating trial of Task 3.

Thus, Task 4 was conducted with offspring from the control and 0.5% groups. Body weights to weaning were not collected during nursing of the second generation, even though mortality in these mice was increased at 4 weeks of age by 15 and 30% for males and females, respectively.

At  $F_1$  mating, mating and fertility indices were equal between the two groups.  $F_2$  pup body weight was reduced by approximately 16%, although litter size and pup viability were unaffected.

After the  $F_2$  litters were evaluated, the  $F_1$  adults were killed and necropsied. Females consuming 0.5% PbA weighed approximately 12% less than controls, and brain weight was approximately 7% less than controls, while adjusted spleen weight was 2.2 times greater than controls. Antemortem estrous cycle evaluations were not performed. For treated males, body weight was reduced by approximately 11%, while absolute testis weight was approximately 9% less than controls. Absolute brain and relative kidney weights were reduced by approximately 5 and 13%, respectively, while relative spleen weight was increased 1.7-fold. Sperm measures were unaffected by PbA consumption.

Thus, this study replicated the Task 2 mortality and pup body weight effects seen in the first study, while showing that lead acetate trihydrate caused reproductive toxicity only in the presence of adult mortality or systemic changes (spleen weight, brain weight changes).

# LEAD ACETATE TRIHYDRATE

**Summary:** NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: PB84208016

Chemical: Lead Acetate Trihydrate

CAS#: 301-04-2

Mode of exposure: Water

Species/strain: Swiss CD-1 mice

F <sub>0</sub> generation	Dose concentration →	0.125%	0.25%	0.5%
General toxicity		Male, female	Male, female	Male, female
Body weight		—, —	—, —	—, —
Kidney weight <sup>a</sup>		•, •	•, •	•, •
Liver weight <sup>a</sup>		•, •	•, •	•, •
Mortality		—, —	—, ↑	—, ↑
Feed consumption		•, •	•, •	•, •
Water consumption		—, —	—, —	—, —
Clinical signs		—, —	—, —	—, —

Reproductive toxicity				
̄ litters/pair		—	—	—
# live pups/litter; pup wt./litter		—, —	—, —	—, ↓
Cumulative days to litter		—	—	—
Absolute testis, epididymis weight <sup>a</sup>		•, •	•, •	•, •
Sex accessory gland weight <sup>a</sup> (prostate, seminal vesicle)		•, •	•, •	•, •
Epidid. sperm parameters (#, motility, morphology)		•, •, •	•, •, •	•, •, •
Estrous cycle length		•	•	•

Determination of affected sex (crossover)	Male	Female	Both
Dose level	•	•	•

F <sub>1</sub> generation	Dose concentration →	•	•	0.5%
General toxicity		Male, female	Male, female	Male, female
Pup growth to weaning		•, •	•, •	—, —
Mortality		•, •	•, •	↑, ↑
Adult body weight		•, •	•, •	↓, ↓
Kidney weight <sup>a</sup>		•, •	•, •	↓, —
Liver weight <sup>a</sup>		•, •	•, •	—, —
Feed consumption		•, •	•, •	•, •
Water consumption		•, •	•, •	—, —
Clinical signs		•, •	•, •	•, •

Reproductive toxicity				
Fertility index		•	•	—
# live pups/litter; pup wt./litter		•, •	•, •	—, ↓
Absolute testis, epididymis weight <sup>a</sup>		•, •	•, •	↓, —
Sex accessory gland weight <sup>a</sup> (prostate, seminal vesicle)		•, •	•, •	—, —
Epidid. sperm parameters (#, motility, morphology)		•, •, •	•, •, •	—, —, —
Estrous cycle length		•	•	—

Summary information	
Affected sex?	Unclear
Study confounders:	None
NOAEL reproductive toxicity:	0.25%
NOAEL general toxicity:	0.125%
F <sub>1</sub> more sensitive than F <sub>0</sub> ?	No
Postnatal toxicity:	Yes

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change (p<0.05); —, —, no change in males or females. <sup>a</sup>Adjusted for body weight.